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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/642,615

08/19/2003

Ali Afzali-Ardakani

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SUITE 200

VIENNA, VA 22182-3817

EXAMINER

GAKH, YELENA G

ART UNIT

PAPER NUMBER

1797

MAIL DATE

DELIVERY MODE

04/30/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/642,615

Applicant(s)

AFZALI-ARDAKANI ET AL.

Examiner

Yelena G. Gakh, Ph.D.

Art Unit

1797

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 March 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3,4,11-13 and 15-18 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3,4,11-13 and 15-18 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SF/08)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Paper No(s)/Mail Date _____
- 6) ☐ Other: _____

DETAILED ACTION

1. RCE field on 03/18/08 and Amendment filed on 02/19/08 are acknowledged. Claims 2, 5-10, 14 and 19-30 are cancelled. Claims 1, 3-4, 11-13 and 15-18 are pending in the application.

Response to Amendment

2. In response to the amendment the examiner withdraws rejection of the claims over the prior art and slightly modifies rejections under 35 U.S.C. 112, first and second paragraphs. Objection to the specification is sustained.

Specification

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to as not enabling obtaining and use of the hypothetical molecules disclosed in the specification as the molecular manipulator. The disclosure describes in general terms the Applicants' hypothesis for a possible molecular manipulator, without any evidence for enabling the Applicants' hypothetical molecule. Moreover, the molecules depicted on Figures 1 and 2 are not CA registered (the library search report is attached) and obviously do not exist. The Applicants did not provide any possible synthetic path for obtaining such molecules, not mentioning their testing as molecular manipulators. The hypothesis is not experimentally proven. The structure indicated as an example cannot be used as a manipulator as disclosed in the specification, since it would have a highly non-planar structure, contrary to what is depicted in the drawings. Moreover, its steric configuration and energetic state would not provide conditions favorable for using such molecules as manipulators as can be clearly seen from the prior art described below, which is especially true for the prophetic example depicted on Figure 2.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 3-4, 11-13 and 15-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Breath of the Claims

The claims recite in the most general terms "a molecule manipulator" comprising a light-sensitive molecule with two azo double bonds which change their configuration upon light irradiation, with the molecule attached to the probe of a scanned-proximity probe microscope. No specifically synthesized molecules, which can act as molecular manipulators as recited in the claims, are disclosed in the specification. The example depicted on Figure 2 is not a real molecule and is not enabled as the molecular manipulator. The specification does not provide any guidance for synthesis of such molecule or any evidence of its ability to act as a molecular manipulator. The structure provided as an example is highly speculative. No other examples besides the fictitious structure are provided in the specification. No guidance for the synthesis of the molecule recited in the claims is provided in the specification. Thus, the claims recite, first, the molecule, which does not exist and the synthesis of which is not disclosed in the specification, and, second, its functional utility as a "molecular manipulator", with no evidence whatsoever that it in fact can be used as the molecular manipulator. The forms depicted in the drawings, which should demonstrate its use as the molecular manipulator, are highly improbable and no evidence exists that they can anyhow be obtained.

The Nature of the Invention

The invention recited in the claims is directed toward a hypothetical molecular manipulator based on a known fact of *cis-trans* light-induced transformation of azo-bond. The only prophetic example for the claimed "manipulator" is depicted as structures on Figures 1A and 2. The *cis*-form drawn on Figure 1A is totally unrealistic because of the severe steric

hindrance, which would be created between two proximate arms. Since the arms can relatively freely rotate about Ph-Ph bonds, the configuration with the two arms turned to each other would be avoided, even if such molecule could be synthesized. Therefore, the specification discloses unenabled utility of the fictitious molecules, with no guidance for the synthesis of this molecule.

The State of the Prior Art

The prior art is in the field of nanotechnology related to “molecular machines” or “molecular tools”. The examiner searched patent and non-patent literature pertinent to molecular tweezers, clips, manipulators, motors, etc. One of the most recent papers on molecular motors, “*Molecular Motor Spins On Surface*” by Netherlands chemists was proclaimed as the “first light-driven molecular rotary motor attached to a solid surface” (*Chemical & Engineering News*, 2005): “by anchoring a chiral helical alkene onto a gold nanoparticle, chemists in the Netherlands have created the first light-driven molecular rotary motor attached to a solid surface (*Nature* 2005, 437, 1337). This mounted molecule, the researchers say, “might be a first step toward the construction of more elaborate and functional nanosized mechanical devices” and perhaps systems to exploit solar energy. Fastening a rotary molecule to something solid, as Ben L. Feringa and colleagues at the University of Groningen have done, brings these spinning systems closer to becoming useful nanomachines. Putting motors on a surface is important because it should make it easier for them to do useful things, like move themselves or cargo, or change the nature of the surface in response to a stimulus,” says T. Ross Kelly, a Boston College chemistry professor who made a molecular motor that runs on chemical fuel. Feringa's team uses two thiol groups to affix their molecular motor to a gold nanoparticle. Two eight-carbon legs link these thiols to the alkene motor. The researchers note that they chose this lengthy anchor to minimize any direct electronic interaction between the alkene and the gold particle. The researchers start the motor's rotation by photoisomerizing the double bond. This forces the methyl group on the molecule's lone stereocenter into an energetically disfavored orientation. When heated, this unstable isomer undergoes a helical inversion, resulting in a net 180° rotation. This step also ensures unidirectional movement. Repeating the two isomerizations completes the 360° revolution”. The molecules have extremely well defined steric structure with experimentally proven behavior as molecular manipulators.

Klärner et al. (Acc. Chem. Res., 2003) provide a detailed review of “Molecular Tweezers and Clips as Synthetic Receptors” with tweezers and clips containing naphthalene and benzene spacer units, which are synthesized by repetitive Diels-Alder reactions. The tweezers and clips should possess specific structural, thermodynamics and other physical-chemical requirements in order for such host-guest interaction to take place: “these molecules are well pre-organized because of their belt-type structures. But bond angle distortions require little energy and, therefore, should induce certain flexibility in these systems, allowing the receptor “arms” to be expanded and compressed during the substrate complexation in a way comparable to the working principle of mechanical tweezers. Thus, a fit of the receptor geometry to the substrate topography to a certain extent, induced by the complex formation, can be expected. The size and shape of the receptor cavities can be systematically varied by varying the number and size of the spacer units. Finally, the parent compounds Ia-Ta are simple hydrocarbons containing only nonconjugated benzene and/or naphthalene rings arranged in a belt-like concave-convex topography, so that an aromatic substrate can be bound via multiple π - π and CH- π interactions” (page 920).

Feringa et al. (Appl. Phys., 2002) describe “Light-driven molecular switches and motors” with detailed disclosing of physical-chemical properties of molecular motors comprising double bond, which undergoes light-induced cis-trans transformation. Specific requirements should be fulfilled for the switches and motors to perform their functions. *Jones et al. and Pearson et al. (J. Org. Chem., 1997)* described in detail “Molecular scale wires with alligator clips” providing their full synthesis and physical-chemical characteristics. A series of papers is devoted to molecular devices based on light-induced cis-trans transformation of azo-bond in azobenzene moieties. *Stiller et al. (Surface and Interface Analysis, 2000)* teach “scanning Kelvin microscopy as a tool for visualization of optically induced molecular switching in azobenzene self assembling films”; *Hugel et al. (Science, 2002)* disclose “single-molecule optomechanical cycle” with a detailed study of molecular devices based on photosensitive azobenzene polymers. *Muraoka et al. (J. Am. Chem. Soc., 2003)* describe “light-driven open-close motion of chiral molecular scissors” based on azobenzene expansion and contraction (cis-trans transformation) of N=N bond. *Jousseime et al. (J. Am. Chem. Soc., 2003)* teach “photomechanical actuation and manipulation of the electronic properties of linear π -conjugated systems” using azobenzene chromophore. *Wen et al. (J. Phys. Chem. B, 2005)* teach “photochemical-controlled switching

based on azobenzene monolayer modified silicon (111) surface". *Bellini et al. (J. Phys.:Condens. Matter, 2006)* disclose "light-induced molecular motion of azobenzene-containing molecules: a random-walk model". None of the recited papers indicate the possibility of using molecules recited in the claims and those depicted on Figures 1 and 2 as molecular manipulators; the examiner did not find any reference, which would disclose a synthesis of similar compounds. The bulkiness of the *cis*-conformer of a hypothetical structure 1A would assume its high non-planarity, which would totally prevent its ability to grab molecules and be used as a molecular manipulator.

The Level of One of Ordinary Skill

The examiner considers synthesis of any of the hypothetic structures disclosed in the specification, including the one depicted on Figure 1A and recited in the claims beyond the skill of a routineer in the art until the Applicants prove otherwise. Obtaining molecules recited in the claims would have been undue experimentation for any routineer in the art. Moreover, even if the synthesis of such structures were possible, it would have been an undue experimentation for a routineer in the art to study these molecules in relation to their ability to be molecular manipulators, especially in light of high improbability of existing structures depicted in Figures 1A, B.

The Level of Predictability in the Art

The prior art does not provide a ground for any expectation of success for using molecules such as depicted on Figure 2, as molecular manipulators. Extensive prior art on molecular manipulators, such as tweezers, scissors, motors, etc., are rigid moelcules with well defined stereometry and thermodynamic parameters. All molecule manipulators have to possess certain characteristics, such as geometrical parameters that fir the molecules do be manipulated. None of the literature references found by the examiner discloses a molecular manipulator with undefined geometry and thermodynamic characteristics. Furthermore, existence of *cis*-configuration depicted on Figure 2, which is a required condition for using the molecule as the molecules manipulator, is highly improbable. The prior art does not predict any utility for the fictitious compounds recited in the claims, not mentioning them being molecular manipulators.

The Amount of Direction Provided by the Inventor

The instant disclosure does not provide any direction for synthesis of the hypothetical structures disclosed in the specification. The instant disclosure does not provide any direction for application of these fictitious structures as molecular manipulators. The specification does not provide any guidance for transferring *trans*-form into *cis*-form as shown in Figure 2, since *cis*-form that is drawn on the Figure is highly improbable because of the steric hindrance and energy requirements; since such structure cannot exist, its application as the molecular manipulator is highly improbable. Thus, the inventors did not provide any guidance for obtaining and utilizing the structure depicted in drawings and recited in the claims.

The Existence of Working Examples

No working examples are provided in the specification for either the synthesis of the compounds disclosed in the specification and their attachment to the microscope probe, or for their application as molecular manipulators. The Applicants did not provide any evidence for the possibility of the structure depicted on Figure 2 to exist in *cis*-form.

***The Quantity of Experimentation Needed
to Make or Use the Invention Based on the Content of the Disclosure***

It would require an undue experimentation for a routineer in the art to synthesize hypothetical compounds disclosed in the specification; it would require even more of undue experimentation to study them as potential molecular manipulators with practically no expectation for success, since the structures do not meet any requirements established by the prior art for the molecular manipulators. Moreover, it seems to be quite improbable for a routineer in the art to obtain any structure similar to the one depicted on Figure 2 as a prophetic example of the claimed molecular manipulators, because the structure can hardly exist in *cis*-form.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1, 3-4, 11-13 and 15-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "a molecular manipulator". It is not clear, what is meant by the term "molecular manipulator" in relation to the compound recited in the body of the claim. It is not clear, how such molecule can be "a molecular manipulator". It is also not clear, how the molecule is attached to the probe.

Response to Arguments

9. Applicant's arguments filed 02/19/08 have been fully considered but they are not persuasive.

In response to the Applicants' remarks that the rejection of the pending claims under 35 U.S.C. 112, first paragraph was withdrawn by the Notice of Panel Decision, the examiner would like to express once more, that withdrawing rejections established in the previous Office action is a formal act for re-opening the prosecution of the case. It is not an indication that the rejection was improper. In the instant case the panel decided to re-open the prosecution of the application, because it has been established that besides rejections under 35 U.S.C. 112, first paragraph, it would be possible to establish rejections over the prior art, which was done in the following Office action. The examiner established rejections under 35 U.S.C. 112, first paragraph, properly using all criteria for this type of rejections, and the panel did not find anything wrong with the rejections. The statement that "the application remains under appeal because there is at least one actual issue for appeal" is used when the rejection remains unchanged. The panel established that *additional* rejection on a different background (obviousness rejection) could be established for the claims pending at that moment, which required re-opening of the application. The examiner respectfully requests the Applicants to provide a paragraph from MPEP, which requires the panel to meet again for repeating decision that was clearly indicated in its first meeting: the rejections are withdrawn and the prosecution is re-opened. Again, the examiner would like to repeat the rule, according to which re-opening the case automatically results in withdrawing the previous rejection. It does not mean that the rejection cannot be re-established with the new rejection added.

The Applicants state in relation to the rejections of the pending claims under 35 U.S.C. 112, first paragraph: "[t]he Examiner, however, is clearly incorrect". Such statement conventionally implies that a detailed and convincing argumentation on the Applicants' side, as to why "the examiner is clearly incorrect", is provided. In the particular case, the examiner did not receive any Applicants' arguments on the essence of the enablement rejections. The examiner was not provided with any evidence that the claimed structures can be synthesized, and that they can be applied as the molecular manipulators, as disclosed in the specification. Instead, all Applicants' argumentation is directed toward the decision of the Panel, of which the examiner is also a member. The examiner does not consider the Applicants' arguments to the enablement rejections as being adequate to the established rejections and respectfully requests to provide such in response to the present Office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yelena G. Gakh, Ph.D. whose telephone number is (571) 272-1257. The examiner can normally be reached on 9:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Yelena G. Gakh/
Primary Examiner, Art Unit 1797

04/24/2008